

AMENDMENTS TO THE SPECIFICATION

Insert the following paragraph at page one of the specification, immediately underneath the title.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the U.S. National Stage of PCT International Application Serial No. PCT/IB2005/002480, filed January 26, 2005, which is a continuation-in-part of U.S. Patent Application Serial No. 10/764,730, filed January 26, 2004.

Amend the paragraph beginning at page 3, line 3, as follows.

Accordingly, the first aspect of the invention features an isolated polypeptide that specifically binds to a neoplastic cell or a cell of a pre-cancerous lesion, but does not specifically bind to a normal cell, where the normal cell is not a cell of the glomerular, fascicular zone of the adrenal gland or an epithelial cell of the collection tubes of the kidney. This isolated polypeptide may include amino acids 28-32, 51-53, and/or 90-100 of the sequence of ~~SEQ ID NO:27~~ SEQ ID NO:29. In desirable embodiments of the first aspect of the invention, the isolated polypeptide also includes amino acids 11-18, 36-43, and/or 82-104 of the sequence of ~~SEQ ID NO:26~~ SEQ ID NO:28. In a related aspect, the invention features an isolated polypeptide that includes amino acids 11-15, 30-46, and/or 79-88 of the sequence of SEQ ID NO:2 and/or amino acids 17-32, 48-54, and/or 87-95 of the sequence of SEQ ID NO:4, but does not include the full-length sequence of SEQ ID

NO:2 or SEQ ID NO:4 and that that specifically binds to a neoplastic cell or a cell of a pre-cancerous lesion, but does not specifically bind to a normal cell, where the normal cell is not a cell of the glomerular, fascicular zone of the adrenal gland or an epithelial cell of the collection tubes of the kidney.

Amend the paragraph beginning at page 3, line 18, as follows.

In other desirable embodiments, the polypeptide includes amino acids 11-18, 36-43, and/or 82-104 of ~~SEQ ID NO:26~~ SEQ ID NO:28 or amino acids 28-32, 51-53, and/or 90-100 of ~~SEQ ID NO:27~~ SEQ ID NO:29, but does not include the full-length amino acid sequence of ~~SEQ ID NO:26~~ or ~~SEQ ID NO:27~~ SEQ ID NO:28 or SEQ ID NO:29.

Amend the paragraph beginning at page 4, line 10, as follows.

In the second aspect, the invention features an isolated nucleic acid molecule containing nucleic acids 31-54, 106-129, and/or 244-312 of the sequence of ~~SEQ ID NO:28~~ SEQ ID NO:26, and/or 82-96, 151-159, and/or 268-300 of the sequence of ~~SEQ ID NO:29~~ SEQ ID NO:27. In desirable embodiments of this aspect, the isolated nucleic acid molecule does not include the full-length sequence or ~~SEQ ID NO:28~~ SEQ ID NO:26 and/or ~~SEQ ID NO:29~~ SEQ ID NO:27. In a related aspect the invention features an isolated nucleic acid molecule containing nucleic acids 31-45, 88-138, and/or 235-264 of SEQ ID NO:1. Desirably, this nucleic acid molecule does not include the full-length

sequence of SEQ ID NO:1. In the third aspect, the invention features an isolated nucleic acid molecule containing nucleic acids 49-96, 142-162, and/or 259-285 of SEQ ID NO:3.

In a desirable embodiment of the third aspect of the invention, the nucleic acid molecule does not include the full-length sequence of SEQ ID NO:3.

Amend the paragraph beginning at page 4, line 22, as follows.

In the fourth aspect, the invention features an isolated nucleic acid molecule including the sequence of SEQ ID NO:5 and in the fifth aspect, the invention features a vector containing the nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, ~~SEQ ID NO:28, and/or SEQ ID NO:29~~ SEQ ID NO:26, and/or SEQ ID NO:27.

Amend the paragraph beginning at page 4, line 26, as follows.

In the sixth aspect, the invention features an isolated cell, e.g., a mammalian cell, containing a vector that includes the nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, ~~SEQ ID NO:28, and/or SEQ ID NO:29~~ SEQ ID NO:26, and/or SEQ ID NO:27.

Amend the paragraph beginning at page 5, line 1, as follows.

In the eighth aspect, the invention features a method of producing the purified polypeptide of the first aspects of the invention. This method involves contacting a cell

with a vector that includes SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, ~~SEQ ID NO:28,~~
~~and/or SEQ ID NO:29~~ SEQ ID NO:26, and/or SEQ ID NO:27 and isolating the
polypeptide expressed by the vector.

Amend the paragraph beginning at page 10, line 1, as follows.

By a “PAM-1 antibody” is meant a polypeptide that specifically binds to the
isoform of CFR-1 that comprises the amino acid sequence of SEQ ID NO:6 and that is
expressed by 23132 cells. In a desirable embodiment, a PAM-1 antibody binds a tumor-
specific glycostructure of the CFR-1 isoform having the amino acid sequence of SEQ ID
NO:6. For example, a PAM-1 antibody may be human monoclonal antibody 103/51,
murine antibody 58-49/69, or a humanized or chimeric antibody containing all or part of
the sequence of SEQ ID NO:2 and/or 4. In further desirable embodiments, a PAM-1
antibody can induce apoptosis or alter proliferation, or both, in a neoplastic cell or a cell
of a pre-cancerous lesion, but not a normal cell. In additional desirable embodiments, a
PAM-1 antibody comprises the amino acid sequence of SEQ ID NO:2 and/or SEQ ID
NO:4 or is encoded, in part, by the nucleic acid sequence of SEQ ID NO:1 and/or SEQ ID
NO:3. In further desirable embodiments, a PAM-1 antibody may comprise amino acids
11-18, 36-43, and/or 82-104 of ~~SEQ ID NO:26~~ SEQ ID NO:28 and/or amino acids 28-32,
51-53, and/or 90-100 of ~~SEQ ID NO:27~~ SEQ ID NO:29.

Amend the paragraph beginning at page 10, line 22, as follows.

Examples of functional fragments of an antibody are V_L, V_H, F_V, F_C, Fab, Fab', or F(ab')₂ fragments which are known to one skilled in the art (see, e.g., Huston et al., Cell Biophys. 22:189-224, 1993; and Harlow and Lane, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, N.Y., 1999). Desirably, a "functional fragment" has an amino acid sequence that is substantially identical to a fragment, e.g., 3, 4, 5, 10, 15, 20, 15, 30, 50, 75, or 100 contiguous amino acids, of the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, ~~SEQ ID NO:26~~ SEQ ID NO:28, or ~~SEQ ID NO:27~~ SEQ ID NO:29. In more desirable embodiments, a "functional fragment" is identical to a fragment of the sequence of SEQ ID NO:2, SEQ ID NO:4, ~~SEQ ID NO:26~~ SEQ ID NO:28, or ~~SEQ ID NO:27~~ SEQ ID NO:29. Such a "functional fragment" may contain 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 15, 30, 50, 75, or 100 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, ~~SEQ ID NO:26~~ SEQ ID NO:28, or ~~SEQ ID NO:27~~ SEQ ID NO:29, or may be the entire amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, ~~SEQ ID NO:26~~ SEQ ID NO:28, or ~~SEQ ID NO:27~~ SEQ ID NO:29. In desirable embodiments, such a fragment includes one or more of the Complement Determining Regions (CDR) of the V_H or the V_L regions of the murine PAM-1 antibody 58-49/69 or human PAM-1 antibody 103/51. For example, a functional fragment may include amino acids 11-15, 30-46, and/or 79-88 of SEQ ID NO:2; and/or amino acids 17-32, 48-54, and/or 87-95 of SEQ ID NO:4. Other examples of functional fragments include

polypeptides having amino acids 11-18, 36-43, and/or 82-104 of ~~SEQ ID NO:26~~ SEQ ID NO:28 and/or amino acids 28-32, 51-53, and/or 90-100 of ~~SEQ ID NO:27~~ SEQ ID NO:29.

Amend the paragraph beginning at page 60, line 26, as follows.

The nucleic acid sequence (~~SEQ ID NO:28~~) (SEQ ID NO:26) and the amino acid sequence (~~SEQ ID NO:26~~) (SEQ ID NO:28) of the variable region of the heavy chain of human antibody 103/51 are shown in Figure 17. CDR1 of the 103/51 variable region heavy chain spans nucleotides 31-54 which encode amino acids 11-18, CDR2 spans nucleotides 106-129 which encode amino acids 36-43, and CDR3 spans nucleotides 244-312 which encode amino acids 82-104.

Amend the paragraph beginning at page 61, line 1, as follows.

The nucleic acid sequence (~~SEQ ID NO:29~~) (SEQ ID NO:27) and the amino acid sequence (~~SEQ ID NO:27~~) (SEQ ID NO:29) of the variable region of the light chain of human antibody 103/51 are shown in Figure 18. CDR1 of the 103/51 variable region light chain spans nucleotides 82-96 which encode amino acids 28-32, CDR2 spans nucleotides 151-159 which encode amino acids 51-53, and CDR3 spans nucleotides 268-300 which encode amino acids 90-100.

Replace the current sequence listing with the sequence listing submitted with the concurrently filed statement under 37 C.F.R. § 1.821.